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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner : David Romeo
Group : 1647
Applicants : John C. Lee et al.
Serial No. : 09/287,500
Filed : April 7, 1999
For : COMPOSITIONS AND THERAPEUTIC METHODS
USING MORPHOGENIC PROTEINS AND
STIMULATORY FACTORS

New York, New York
April 19, 2004

Hon. Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF JOHN C. LEE
UNDER 37 C.F.R. ' 1.132

I, JOHN C. LEE, hereby declare and state as
follows:

1. I am one of the co-inventors of the subject
matter of the above-identified application.

2. I am currently a Professor in the Department of Biochemistry at the University of Texas Health Science Center at San Antonio, TX. I have held this position since 1985. From 1966 to 1985, I held several positions, including Assistant and Associate Professor in the Department of Biochemistry at the University of Texas and Health Sciences Center at San Antonio, TX, Instructor in the Department of Biology at Massachusetts Institute of Technology, Cambridge, MA and Lecturer at Taylor University, Indiana. I received my Ph.D. from Purdue University, Indiana, in 1966. I was a research fellow from 1966 to 1968 in the Department of Biochemistry at Massachusetts Institute of Technology, Cambridge, MA. I have published over 79 scientific papers in peer reviewed journals. A copy of my curriculum vitae is attached as Exhibit A.

3. I have devoted a substantial portion of my scientific work to studying the effect of morphogenic proteins in conjunction with growth factors, hormones and cytokines.

4. I have read the November 17, 2003 Office Action ("Action") in the above-identified application. The

Examiner states that the claims are directed to or encompass the induction of endochondral or intramembranous bone, or cartilage, or tendon/ligament-like and neural tissue with a morphogen and synergistic enhancement of the morphogen's tissue induction with a MPSF, but that the only working example is the induction of alkaline phosphatase ("AP") activity in FRC cells. I make this declaration in response to the above statement.

5. In addition to the experiments described in the above application which show that IGF-I is capable of synergistically enhancing the bone inducing activity of OP-1, as demonstrated by induction of alkaline phosphatase, I have also demonstrated that IGF-I can synergistically enhance OP-1's cartilage inducing activity.

6. I have attached hereto, as Exhibits B and C, the description of an experiment to demonstrate the synergistic effect of OP-1 in combination with IGF-I on cartilage formation and the results thereof.

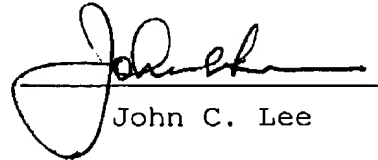
7. Exhibit B describes the test materials and experimental design. I conducted this experiment using bovine articular cartilage ("BAC") primary culture cells. The

methods used in this experiment are similar to those described in the above-identified application.

8. Exhibit C shows the results of the combination of OP-1 and IGF-I on AP activity in BAC cells. Specifically, the AP activity in BAC cells treated with the combination of OP-1 and IGF-I was 6.09 whereas the AP activity for IGF-I-treated and OP-1-treated cells were 1.35 and 2.92, respectively. These results demonstrate that the combination of OP-1 and IGF-I synergistically enhance the AP activity in bovine articular cartilage cells. It is my opinion that this assay is predictive of *in vivo* cartilage formation. Moreover, these results demonstrate that the synergistic effect of IGF-I on OP-1's tissue inductive activity is not limited to bone tissue but is also present in cartilage tissue.

9. I declare further that all statements made herein of my own knowledge are true and that all statements made herein on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under

Section 1001, Title 18, United States Code and that such willful false statements may jeopardize the validity of this application and any patent issuing thereon.



John C. Lee

Signed at San Antonio, Texas
this 19 day of April, 2004.

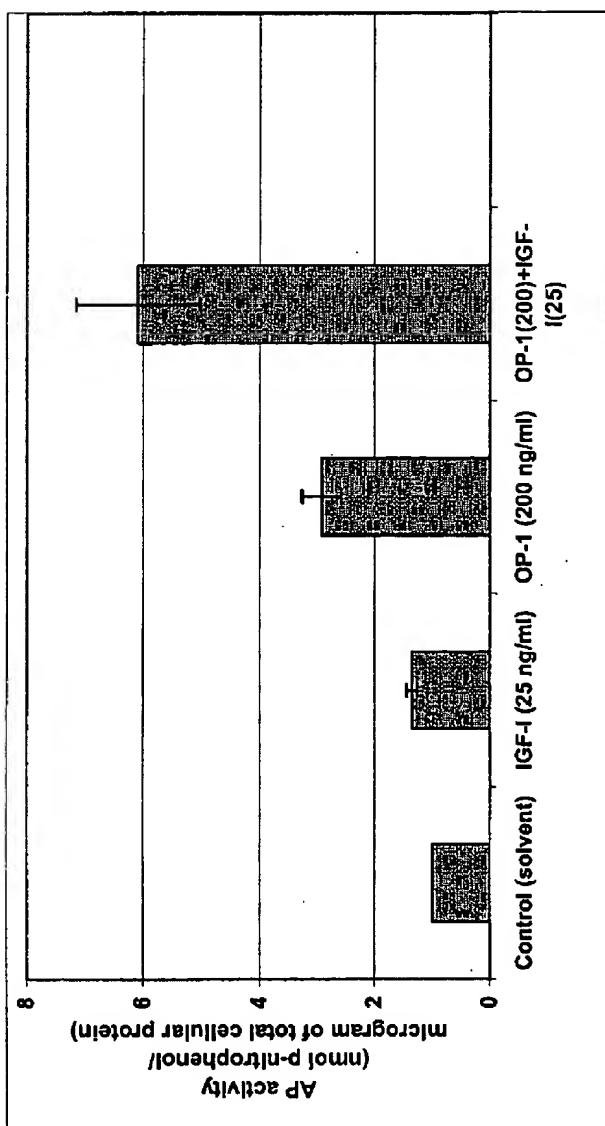
Exhibit B**Test Materials and Experimental Design**

Primary bovine articular cartilage ("BAC") cell cultures were prepared using mainly published procedures (Luyten, F.P. et al., Expt. Cell Res., 21, pp. 224-229 (1994); Martin, I. et al., Expt. Cell Res., 253, pp. 681-688 (1999)). Briefly, cells were harvested by digestion of slices of freshly collected bovine cartilage with sterile, 0.2% collagenase (Life Technologies, Grand Island, NY) in Hanks' Balanced Salt Solution (HBSS) plus penicillin/streptomycin (100 U/ml/100µg/ml) overnight at 37°C. Cells were washed several times with Dulbecco's modified Eagle Minimum Essential Medium (D-MEM, Life Technologies, Grand Island, NY), containing 10% fetal bovine serum (FBS), gentamicin (30µg/ml) and fungazone (3µl). BAC cell cultures were plated in D-MEM media containing 10% fetal bovine serum, gentamicin (30µg/ml) and fungazone (3µl). Cultures were incubated at 37°C with 95% air/5% CO₂ for several days to reach confluence. Cells were then subcultured for experimentation.

BAC cells were subcultured in 48-well plates (Costar) in complete D-MEM medium with 10% fetal bovine serum until confluent in about 4-5 days. Confluent cells were rinsed with PBS and treated with serum-free D-MEM medium (with 0.1% BSA, 100U/ml penicillin, and 100 mg/ml streptomycin) containing the appropriate solvent vehicle, or recombinant human OP-1, IGF-I or the combination of OP-1/IGF-I as described in the above-identified application. At the end of treatment, BAC cells were lysed and total cellular alkaline phosphatase activity was measured as described in the above-identified application (typically after 48 hours of treatment).



Exhibit C



April 16, 2004



Exhibit A

CURRICULUM VITAE

John Chung Lee

I. GENERAL INFORMATION

A. Personal Data:

1. Citizenship Status: U.S. Citizen

B. Education:

- 1966 Ph.D. Molecular Biology, Purdue University, Indiana (Advisor: Dr. P. Gilham)
- 1964 M.Sc. Biophysics, Purdue University, Indiana (Advisor: Dr. W. Ray)
- 1961 B.A. Physics/Mathematics, Taylor University, Indiana

C. Post-Graduate Training:

- 1966-68 Postdoctoral, Biochemistry, Massachusetts Institute of Technology, Cambridge, MA (Mentor: Dr. V.M. Ingram)

D. Academic Appointments:

- 9/1985 - present Professor, Department of Biochemistry,
The University of Texas Health Science Center at San Antonio
- 9/1972 - 8/1985 Associate Professor, Department of Biochemistry,
The University of Texas Health Science Center at San Antonio
- 10/1969 - 8/1972 Assistant Professor, Department of Biochemistry,
The University of Texas Health Science Center at San Antonio
- 9/1968 - 9/1969 Instructor, Department of Biology, Massachusetts Institute of
Technology
- 9/1966 - 12/1966 Lecturer, Taylor University, Indiana

E. Other Employment: None

F. Certification and Licensure: None

G. Honors and Awards:

- 1985 Travel Award from American Society of Biological Chemists to attend the
13th International Congress of Biochemistry
- 1977 Max Planck Institute (Germany) Fellow

- 1976 Alexander von Humboldt Foundation (Germany) Research Fellowship (declined to accept the Max Planck Institute Fellowship)
- 1976 Travel Award from American Society of Biological Chemists for attending the Xth International Congress of Biochemistry
- 1961 B.A. cum laude, Taylor University
- 1960 Who's Who in American Colleges and Universities

Teaching honors:

- 1990 Nominated for the Presidential Teaching Award, UTHSCSA
- 1986 Received a Certificate of Appreciation from the Medical Class of '88.

II. TEACHING

a) Classroom/Laboratory:

Have taught yearly in Medical Biochemistry (200 students), Dental Biochemistry (100 students), and various advanced graduate level courses (15 to 45 students) since 1971.

b) Clinical Teaching: N/A

c) Instructional Development:

1. Formal Study to Improve Teaching Abilities:

- 1983 Took 2 courses offered by Continuing Education, UTHSCSA on Test Construction and Handout Preparation.
- 1966 Successfully completed a graduate course on Instructional Methods, Purdue University.

2. Current Research Concerning Teaching: None

3. Bibliography Concerning Teaching: None

4. Media and Software Developed:

As a consultant in the production of two educational films - "Replication of Genetic Materials" (Producer-Dr. Burton)

d) Master's Theses and Ph.D. Dissertations - Directed, Membership on Supervising Committees, and Postdoctoral Fellows Supervised:

1. As Supervising Professor:

<u>Name</u>	<u>Degree/date</u>	<u>Current position</u>
Martinez, Yoland	M.S./May, 1973	Retired
Henderson, A.Burl.	Ph.D./May, 1976	VP, Univ. TX at Arlington
Wood, Katharine.O.	Ph.D./May, 1978	VP Research, Genzyme, MA

Pickett, Steve	Ph.D./May, 1982	Private practice
Thweatt, Ray	Ph.D./May, 1990	Professor, Comm. Col. Southern Nevada
Tian, Jiandong	Ph.D. candidate	(Left for another university in 1993)
Tziotis, Vassili	Ph.D. candidate	(returned to Greece without a degree)
Villerreal, Jactino	M.S./May, 1997	Practicing pharmacist
Knecht, Evangeline	M.S./December, 1998	Research Scientist, Merck
Yin, Huiran	Ph.D. candidate	Current

2. As A Member of the Supervising Committee:

Have served on Master or Ph.D. student Supervising Committees for 40 students from Biochemistry, Microbiology, Anatomy of UTHSCSA, UTSA and Univ. North Texas since 1975.

Current:

Robin, Howard, M.S. candidate	Microbiology, UTHSCSA
Zepeda, Rachel, M.S. candidate	Microbiology, UTHSCSA
Ogg, Monica, Ph.D. candidate	Microbiology, UTHSCSA
Zuniga, Jorge, Ph.D. candidate	Biochemistry, UTHSCSA
Siller-Jackson, Arlene, Ph.D. candidate	Biochemistry, UTHSCSA
Joe, Patrick, Ph.D. candidate	Biochemistry, UTHSCSA
Kaur, Yogeet, Ph.D. candidate	Biochemistry, UTHSCSA
Vogt, Rhonda, M.S. candidate	Biology, Univ. TX at San Antonio

3. Postdoctoral Trainees and Visiting Scientists:

Batterton, John (Ph.D., University of Texas at Austin)	1973-1975
Erck, Anna (Ph.D., University of Houston)	1975-1979
Xiang, R. H. (M.D., Peoples Republic of China)	1986-1989
Li, T.L. (M.D., Peoples Republic of China)	1989-1990
Chang, S. I. (M.D., Peoples Republic of China)	1990-1991
Tsay, Y-F. (Ph.D., Carnegie Mellon University, PA)	1992-1992
Shahed, Asha (Ph.D.)	1993-1994
Son, Marjatta (Ph.D.)	1993-1995
Krakower, Terri (Ph.D., University of Texas at Austin)	1994-1996
Pakhomova, Olga (Ph.D., Med. Rad. Res. Ctr, Obninsk, Russia)	1997-1999
Mikhailov, Valery I (M.D., Moscow Medical Institute, Ph.D., Institute of Biol. Med. Chem. Moscow, Russia)	1998-1999
Unda, Richard (Ph.D., Medical College of Georgia)	1996-2000
Yeh, L-C. Caroline (Ph.D., University of Oregon)	1985-present
Shibatani, Toru (Ph.D., UTHSCSA)	1999-2001
Shoba, Lungile (Ph.D., Northwestern University)	2000-2002
Tsin, Andrew, Ph.D., Professor, UTSA	1999-present
(Dr. Tsin comes and works in my lab a few hours each week during the fall and spring semester. He works full time during the summer months. I am serving as Dr. Tsin's sponsor for his NIH career development award)	
Chen, Jianlin (M.D., Ph.D., PPR)	2001-2002
Zhou, Qing (Ph.D., PPR)	2001-present

4. As a member of the Ph.D. degree candidacy preliminary examination committee (last three years):

Have served on preliminary examination committee of 6 students

5. As supervisory professor during student's first year rotation (last 5 years)

Contreras, Veronica
Yin, Xinye
Song, Dong-Weon
Zhong, Ming (Spring 2001)
Zhou, Yue (Spring 2001)
Huiran Yin (Fall 2001)

III. RESEARCH

A. Bibliography:

1. Books and/or Chapters :

Lee, J.C. (1979) *Fetal Hemoglobin in Women with Hydatidiform Molar Pregnancy*. In "Cellular and Molecular Regulation of Hemoglobin Switching" Ed. by G. Stamatoyannopoulos and A.W. Nienhuis. Grune and Stratton, New York, p. 133-138.

Lee, J. C. *The Ribosome*. In "The Yeasts", ed. by J. S. Harrison and A. H. Rose (2nd Edition) (1991) Academic Press, New York, Vol. 4, 489-539.

Ticku, M.K., Lee, J.C., Murk, S., Mhatre, M.C., Story, J.L., Kagan-Hallet, K., Luther, J.S., and Eidelberg, E. (1992) *Inhibitory and excitatory amino acid receptors, c-fos expression, and calcium-binding proteins in the brain of baboons (Papio cynocephalus) that exhibit "spontaneous" grand mal epilepsy*. In "Molecular neurobiology of Epilepsy" ed. by G. Aranzini, E.A. Cavalheiro, U. Heinemann, C. Westerlain, and J. Engel, Jr. Elsevier Science Publ. pp. 141-149.

Yeh, L-C.C. and Lee, J.C. (1995) *Role of Specific Amino Acids in Yeast Ribosomal Protein L1 in RNA Recognition*. Protein Engineering and Structural Biology. IRL Press. vol. 8, 7-8.

Lee, J.C. and Yeh, L-C. C. (1995) *Involvement of multiple basic amino acids in yeast ribosomal protein L1 in 5S rRNA recognition*. Nucleic Acids Res. Symposia Series, vol.33, 63-65.

Lee, J.C. and Yeh, L-C. C. (2004) *Synergy between Osteogenic Protein-1 and osteotropic factors in the stimulation of rat osteoblastic cell differentiation*. In "The Skeleton: Biochemical and Molecular Interactions in Development and Homeostasis". Ed. By E.J. Massaro and J. M. Rogers. Humana Press, Inc., NY. Pp. 173-183

2. Papers published or in Press (* denote refereed journals):

1. *Lee, J.C., Ho, N.W.Y. and Gilham, P.T. (1965) *Preparation of Ribotrinucleotides Containing Terminal Cytidine*. **Biochem. Biophys. Acta.** 95, 504.
2. *Lee, J.C. and Gilham, P.T. (1965) *Determination of Terminal Sequences in Viral and Ribosomal Ribonucleic Acids*. **J. Am. Chem. Soc.** 87, 4001.

3. *Lee, J.C. and Gilham, P.T. (1966) *A Method for the Determination of Nucleotide Sequences near the Terminals of Ribonucleic Acids of Large Molecular Weight.* **J. Am. Chem. Soc.** 88, 5685-5686.
4. *Lee, J.C. and Ingram, V.M. (1967) *Erythrocyte Transfer RNA: Change during Chick Development.* **Science** 158, 1332.
5. *Lee, J.C. and Ingram, V.M. (1969) *Reaction of 5S RNA with a Radioactive Carbodiimide.* **J. Mol. Biol.** 41, 441.
6. *Lee, J.C., Weith, H.L. and Gilham, P.T. (1970) *Isolation and Characterization of Terminal Polynucleotide Fragments from Bacteriophage Ribonucleic Acids.* **Biochemistry** 9, 118.
7. Kennedy, W. and Lee*, J.C. (1970) *Separation of Mono- and Di-ribonucleotides and Deoxymononucleotides by High Speed Liquid Column Chromatography.* **J. Chromatog.** 51, 209.
8. *Lee, J.C. (1971) *Preparation and Properties of a Water-Insoluble Derivative of Ribonuclease T1.* **Biochim. Biophys. Acta.** 235, 441.
9. Grinnell, F. and *Lee, J.C. (1972) *Alterations in the Rate of Hemoglobin Synthesis during Chick Embryogenesis.* **J. Cellular Physiology** 79, 116.
10. Quintanilla, I.V. and *Lee, J.C. (1972) *Effects of Ribonuclease T1 on E. coli Ribosomes.* **Biochemistry** 11, 1363.
11. *Lee, J.C. and Quintanilla, I.V. (1973) *Terminal Sequences of Oligonucleotides from Ribonuclease T1 Digested E. coli Ribosomes.* **Biochem. Biophys. Res. Commun.** 51, 19.
12. *Lee, J.C. (1976) *Polyadenylic Acid-containing RNA and Poly A Polymerases in Developing Chick Erythrocytes.* **Arch. Biochem. Biophys.** 116, 690-699.
13. Henderson, A.B. and Lee, J.C. (1976) *Cell-free Protein Synthesizing Systems from Developing Chick Embryos.* *Texas J. Sci. Spec. Publ.* 1, 141-148.
14. Henderson, A.B. and Lee*, J.C. (1976) *Hemoglobin Transition in Erythrocytes of Developing Chick. I. Studies with Cell-Free Protein Synthesis Systems.* **Arch. Biochem. Biophys.** 174, 646.
15. *Lee, J.C. and Roach, M. (1975) *Formation of Aminoacyl-tRNA-guanylyl-5'methylene Diphosphonate-elongation Factor Complex.* **Biochem. Biophys. Res. Commun.** 63, 869.
16. *Lee, J.C. (1975) *Base Composition of Terminal Polynucleotides Isolated from Mouse Ascites Nucleolar RNA.* **Biochem. Biophys. Res. Commun.** 66, 1262.
17. Wood, K.O. and Lee*, J.C. (1976) *Integration of Synthetic Globin Genes into an E. coli Plasmid.* **Nucleic Acids Research** 3, 1961-1971.
18. Brawner, T.A., Lee*, J.C. and Trent, D.W. (1977) *A Comparison of Saint Louis Encephalitis and Sindbus Virus RNA.* **Arch. Virology** 54, 147-153.

19. Erck, A., and Lee, J.C. (1978) *Effect of Hemin on Cell-free protein Synthesis in Avian Reticulocytes*. Texas J. Sci. Spec. Publ. 4, 149-154.
20. Wood, K.O. and Lee, J.C. (1978) *Expression of A Rabbit Globin Gene-containing Hybrid Plasmid in E. Coli*. Texas J. Sci. Spec. Publ. 4, 149-154.
21. Pickett, S. and Lee, J.C. (1978) *Phosphorylation of Ribosomal and Ribosome-associated Proteins in Developing Cardiac Hypertrophy*. Texas J. Sci. Publ. 4, 95-105.
22. Lee*, J.C. (1981) *Inhibition of Hemoglobin Production in Chick Embryos by Arabinosyl Cytosine*. **Cytobios** 31, 37-47.
23. *Lee, J.C., Shephard, M.K. and Hayashi, R.H. (1982) *Hemoglobin F, F-cells and Hormone Levels in Women with Normal and Hydatidiform Molar Pregnancy*. **Amer. J. Hematology** 13, 131-139.
24. *Lee, J.C. and Gauntt, C.J. (1982) *Human Interferon Alters Phosphorylation of Ribosomal Proteins*. **J. Interferon Res.** 2, 345-354.
25. *Lee, J.C. and Henry, B. (1982) *Binding of Rat Liver Ribosomal Proteins to Yeast 5.8S RNA*. **Nucleic Acids Res.** 10, 2199-2207.
26. Michel, S., Traut, R.R., and Lee*, J.C. (1983) *Yeast Ribosomal Proteins: Electrophoretic Analysis in Four Two-dimensional Gel Systems: Correlations of Nomenclature*. **Molecular General Genetics** 191, 251-256.
27. *Lee, J.C. and Haley, W.J. (1983) *Reactivity of Proteins in Ribosomes from *Saccharomyces cerevisiae* with Trypsin*. **Arch. Biochem. Biophys.** 224, 69-76.
28. Roodman, G.D., *Lee, J.C. and Gidari, A.S. (1983) *Effects of Dexamethasone on Erythroid Colony and Burst Formation from Human Foetal Liver and Adult Marrow*. **Brit. J. Haemat.** 53, 621-628.
29. Gauntt, C.J. , Trousdale, M.S. , *Lee, J.C., Paque, R.E. (1983) *Preliminary Characterization of Coxsackievirus B3 ts mutants*. **J. Virology** 45, 1037-1047.
30. Paque, R.E. and *Lee J.C. (1983) *Acrylamide Gel Analysis of Sucrose Gradient derived RNA B-fractions Transferring Delayed Sensitivity in vitro*. **Cell Immunol.** 78, 342-355.
31. *Lee, J.C., Henry, B. and Yeh, Y-C. (1983) *Binding of Proteins from the Large Ribosomal Subunits of *Saccharomyces cerevisiae* to the 5.8S RNA*. **J. Biol. Chem.** 258, 854-859.
32. *Lee, J.C. (1984) *Preliminary Characterization of Protein Synthesis Initiation Factor eIF-2 from Chicken Reticulocytes*. **International J. Biochem.** 16, 1143-1147.
33. *Lee, J.C. and Traut, R.R. (1984) *Proximity of 5.8S RNA-binding Proteins and A-site Proteins in Yeast Ribosomes Inferred from Crosslinking*. **J. Biol. Chem.** 259, 9971-9974.
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35. *Lee, J. C., Anderson, R., Yeh, Y. C., and Horowitz, P. (1985) *Extraction of Proteins from Ribosomal Subunits of Saccharomyces cerevisiae under non-denaturing conditions.* **Arch. Biochem. Biophys.** 237, 292-299.
36. Francouer, A. M., Peebles, C. L., *Lee, J. C., and Tan, E. M. (1985) *Identification of Ribosomal Protein Autoantigens.* **J. Immunol.** 135, 2378-2384.
37. Pickett, S. and *Lee, J. C. (1985) *Phosphorylation of Ribosomal and Ribosome associated Proteins in Isoproterenol-induced Cardiac Hypertrophy.* **International J. Biochemistry** 17, 1019-1022.
38. *Lee, J. C. and Anderson, R. (1986) *Partial Reassembly of Active Yeast Ribosomal Subunits following Controlled Dissociation under Non Denaturing Conditions.* **Arch. Biochem. Biophys.** 245, 248-253.
39. Yeh, Y. C., Traut, R. R., and *Lee, J. C. (1986) *Protein Topography of the 40S Ribosomal Subunit from Saccharomyces cerevisiae as shown by Chemical Crosslinking.* **J. Biol. Chem.** 261, 14148-14153.
40. *Lee, J. L. and Horowitz, P. (1987) *Tritium exchange kinetics of yeast ribosomal subunits.* **Biochim. Biophys. Acta** 908, 109.
41. *Lee, J. C., Kuehl, T., and Roodman, D. G. (1987) *Developmental Changes in Membrane Proteins from Baboon Erythrocytes.* **Comparative Biochemistry and Physiology** 88B, 233-236.
42. Lam, K. W., Sieman, M., *Lee, J. L., Yam, L. T., Li, C. Y., and Wold, L. E. (1987) *The Clinical Significance of Tartrate Sensitive and Tartrate Resistant Acid Phosphatase Indicated from the Study of Their Biosynthetic Mechanism.* **Clinical Physiology and Biochemistry** 5, 305-314.
43. Yeh, L-C. C., Lee, A. J., Lee, N. E., Lam, K. W., and *Lee, J. C. (1987) *Molecular Cloning of cDNA for Human Acid Phosphatase Isoenzyme 2.* **Gene** 60, 191-196.
44. Yeh, L-C. C., Horowitz, P. M., and Lee, J. C. (1988) *Studies of RNA-Protein Interactions in the Yeast Ribonucleoprotein Particles by Fluorescence and Tritium Exchange.* ICSU Short Reports, Advances in Gene Technology: Protein Engineering and Production, Ed. K. Brew, F. Ahmad, H. Bialy, S. Black, R. Fenna, D. Puett, W. A. Scott, J. Van Brunt, R. W. Voellmy, W. J. Whelan, and J. F. Woessner. IRL Press, Vol. 8, p. 84.
45. Yeh, L-C. C., Horowitz, P. M., and *Lee, J. C. (1988) *Studies of RNA-Protein Interactions in the Yeast 5S Ribonucleoprotein Particles by Fluorescence and Tritium Exchange: Implications for Ribosomal Assembly.* **J. Biol. Chem.** 263, 17412-17417.
46. Yeh, L-C. C. and *Lee, J. C. (1988) *Probing the Higher Order Structure of the Yeast 5S RNA in the Ribonucleoprotein Complex with Fluorescence and Ribonuclease.* **J. Biol. Chem.** 263, 18213-18219.
47. Xiang, R. H. and *Lee, J. C. (1989) *Protein Topography in Yeast 60S Ribosomal Subunits are revealed by Chemical Crosslinking.* **J. Biol. Chem.** 264, 10542-10546.
48. Xiang, R. H. and *Lee, J. C. (1990) *Identification of Proteins Crosslinked to RNA in the 40S Ribosomal Subunits of Saccharomyces cerevisiae.* **Biochimie** 71, 11-14.

49. Thweatt, R. and *Lee, J. C. (1990) *Yeast Precursor Ribosomal RNA. Molecular Cloning and Probing the Higher-order Structure of the Internal Transcribed Spacer 1 by Kethoxal and Dimethylsulfate Modification.* **J. Mol. Biol.** 211, 305-320.
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51. Yeh, L-C. C. and *Lee, J. C. (1990) *Structural Analysis of the Internal Transcribed Spacer 2 of the Precursor Ribosomal RNA from Saccharomyces cerevisiae.* **J. Mol. Biol.** 211, 699-712.
52. *Lee, J. C. and Braun, A. (1990) *Analysis of Rat Hindlimb Muscle Proteins by Two-dimensional Gels following Spinal Cord Injury.* **J. Neurochem.** 54, 96-101.
53. *Lee, J. C. and Braun, A. (1990) *Changes in Muscle Proteins following Different Neural Lesions.* **Clinical Physiology and Biochemistry**, 8(3), 116-121.
54. Yeh, L-C. C., Thweatt, R., and *Lee, J. C. (1990) *Internal transcribed spacer 1 of the yeast precursor ribosomal RNA. Higher order structure and common structural motifs.* **Biochemistry** 29, 5911-5918.
55. Yeh, L-C. C. and *Lee, J. C. (1991) *Higher order structure of the 5.8S rRNA sequence within the yeast 35S precursor ribosomal RNA synthesized in vitro.* **J. Mol. Biol.** 217, 649-659.
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58. Yeh, L-C.C. and *Lee, J.C. (1992) *Higher order structure of the 5'-external transcribed spacer of the yeast precursor ribosomal RNA.* **J. Mol. Biol.** 228, 827-839.
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61. Yeh, L-C. C. and *Lee, J. C. (1995) *Contributions of multiple basic amino acids in the c-terminal region of yeast ribosomal protein L1 to 5S rRNA binding and 60S ribosome stability.* **J. Mol. Biol.** 246, 295-307.
62. Deshmukh, M., Stark, J., Yeh, L-C. C., *Lee, J.C., and Woolford, J.L., Jr. (1995) *Multiple regions of yeast ribosomal protein L1 are important for its interaction with 5S rRNA and assembly into ribosomes.* **J. Biol. Chem.** 270, 30148-30156

63. Son, M., Shahed, A.R., Werchan, P.M., and *Lee, J.C. (1995) *c-fos and HSP70 gene expression in rat brains in high gravitation-induced cerebral ischemia. Neurosci. Lett.* 200, 81-84.
64. Kitten, A.M., *Lee, J.C., and Olson, M.S. (1995) *Osteogenic protein 1 enhances phenotypic expression in ROS 17/2.8 cells. American J. Physiol.* 269 (Endocrinol. Metab. 32): E918-E926
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83. Yeh, L-C. C., Tsai, A.D., and *Lee, J. C. (2002) *Osteogenic Protein-1 (OP-1, BMP-7) induces osteoblastic cell differentiation of the pluripotent mesenchymal cell line C2C12.* **J. Cell. Biochem.** 87, 292-304
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3. **Meeting abstract**

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35. Thweatt, R. and Lee, J. C. Comparison of SP6 and T7 RNA Polymerase in the Production of High Molecular Weight Yeast Precursor Ribosomal RNA. Presented at the 1986 Lost Pines Molec. Biol. Conferences, October, 1986, The University of Texas Cancer Center, Smithville, TX (1986).
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39. Yeh, L-C. C. and Lee, J. C. Higher order structure of the internal transcribed spacers of the Yeast precursor ribosomal RNA. ASM Conference on ribosomes, MT (1989).
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42. Yeh, L-C. C. and Lee, J. C. Selectivity in binding of ribosomal proteins by yeast 35S precursor RNA. Poster Presentation in Cold Spring Harbor meeting on Ribosome Synthesis. (1991).
43. Lee, J.C. and Horowitz, P.M. Tryptophan fluorescence of the yeast 5S rRNA-L1a protein complex. *The FASEB J.* 6, A66 (1992).
44. Yeh, L-C. C., Corder, T. S. and Lee, J. C. Interactions between yeast ribosomal protein L1a and 5S rRNA as revealed by site-directed mutagenesis. *The FASEB J.* 6, A66. (1992).
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47. Yeh, L-C.C., Bernstein, P.L., Ross, J., and Lee, J.C. The higher order structure of a region of the human *c-myc* mRNA that binds to a protein capable of affecting its half life. The FASEB J. 7, A1293 (1993)
48. Lee, J.C., and Yeh, L-C.C. Functional role of lysine residues on the yeast ribosomal protein L1a as revealed by site-directed mutagenesis. The FASEB J. 7, A1093 (1993)
49. Yeh, L-C. C. and Lee, J.C. Binding of RNA by the yeast ribosomal protein L1a involves several lysine and arginine residues located on one side of a helix. Present at the ASBMB meeting, May 21-25, 1994.
50. Son, M., Shahed, A.R., Werchan, P.M., and Lee, J.C. C-fos expression in rat brains in response to + Gz-induced cerebral ischemia. Present at the ASBMB meeting, May 21-25, 1994.
51. Krakower, T.J., Yeh, L-C.C., and Lee, J.C. Mutations in the putative bipartite nuclear localization sequence of yeast ribosomal protein L1 decreases its binding to 5S rRNA. The FASEB J. 9, A1278 (1995).
52. Yeh, L-C.C., Adamo, M.L., Kitten, A.M. Olson, M.S. and Lee, J.C. Changes in IGF-I expression in OP-1-treated fetal rat calvarial cells. J. Bone & Min. Res. 10, suppl. 1, S245 (1995)
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54. Kitten, A.M., Yeh, L-C.C., Lee, J.C., and Olson, M.S. OP-1 and endothelin synergistically activate early response genes in osteoblasts. J. Bone & Min. Res. 10, suppl. 1, S256 (1995)
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56. Yeh, L-C.C., Olson, M.S., and Lee, J.C. Effects of OP-1 on serine/threonine kinase receptor gene expression in osteoblastic cells. J. Bone & Mon. Res. J. Bone & Min. Res. 11, suppl 1, T306 (1996)
57. Yeh, L-C.C., Adamo, M.L., and Lee, J.C. Different mechanisms are used to regulate IGF-I, IGF-II and IGFBP-5 gene expression in primary bone cell cultures by Osteogenic protein-1. Second International Conference on Bone Morphogenetic Proteins. (1997)
58. Yeh, L-C. C., and Lee, J.C. Contributions of specific amino acids in yeast ribosomal protein L1 in RNA recognition. FASEB (1997)

59. Yeh, L-C. C. and *Lee, J.C. (1998) *Yeast ribosomal proteins L4, L17, and L20 exhibit different binding characteristics for the yeast 35S precursor rRNA*. Proteins that bind RNA Conference May 1997. NJ
60. Pakhomova, O., Yeh, L-C.C. and Lee, J.C. (1998) Proteins that bind RNA Conference May 1997. NJ
61. Yeh, L-C. C., Unda, Richard, and *Lee, J.C. (1999) Osteogenic protein-1 differentially regulates the mRNA levels of bone morphogenetic protein-2,-4,-5, and -6 in primary cultures of osteoblasts from fetal rat calvaria and tibia. 81st Ann. Mtg of The Endocrinology Society, June 1999 San Diego, CA
62. Yeh, L-C. C. and *Lee, J.C. (1999) Identification of basic fibroblast growth factor responsive elements in the rat insulin-like growth factor binding protein-5 gene. The FASEB J.
63. Tsin, A., Villazana, E., Muniz, A., Lopez-Cruzman, M., Vidro, E. and *Lee, J.C. (2000) 11-cis retinyl ester hydrolase activity in cultured human retinal pigment epithelial cells. Abstract. Association for Research in Vision and Ophthalmology, Fl, May 2000
64. Yeh, L-C. C., Mikhailov, V. and *Lee, J.C. (2000) Regulation of expression of plasminogen activator inhibitor-1 and tissue inhibitor of metalloproteinase-2 in rat osteoblasts by osteogenic protein-1. Amer. Soc. Bone Miner. Research 22nd Ann. Mtg. Toronto, Canada Sept. 22-26,2000
65. Tsin¹, A.T.C., Unda¹, R., Villazana¹, E.T., Ghaffari¹, S., Yeh², L-C.C., Lee², J.C. and Ma³, J-X. University of Texas at San Antonio¹; University of Texas Health Science Center at San Antonio²; Medical University of South Carolina³. (2000) Human Retinal Pigment Epithelial Cells Cultured in Two Glucose Concentrations. Abstract. Association for Research in Vision and Ophthalmology, Fl, May 2001
66. Yeh, L-C. C., Lin, M., Song, D-W. and *Lee, J.C. Involvement of Arginine 23 and Arginine 24 of Yeast 5S rRNA Binding Protein in Ribosome Assembly. FASEB March 2001.
67. Yeh, L-C. C., and *Lee, J.C. Regulation of the cloned aggrecan gene promoter by Osteogenic Protein-1 (OP-1, BMP-7). ASBMR 24th Annual Meeting, San Antonio, 2002
68. Tsai, A. D., Yeh L-C. C. and *Lee, J.C. Effects of Osteogenic Protein-1 (OP-1, BMP-7) on Medial Collateral Ligament Cells in culture. ASBMR 24th Annual Meeting, San Antonio, 2002
69. Yeh, L-C. C., Tsai, A.D., and *Lee, J.C. Osteogenic Protein-1 (OP-1, BMP-7) induces osteoblastic cell differentiation of the pluripotent mesenchymal cell line C2C12. The Endocrine Society 84th Annual meeting, San Francisco, 2002
70. Shoba, S.N.N. and *Lee, J.C. Inhibition of phosphatidylinositol 3-kinase and p7-S6 kinase blocks Osteogenic Protein-1 induction of alkaline phosphatase activity in fetal rat calvaria cells. The Endocrine Society 84th Annual meeting, San Francisco, 2002
71. Yeh, L-C. C., Tsai, A.D., and *Lee, J.C. Osteogenic Protein-1 Induces Differential Gene Expression Of BMP And GDF Family Members In Medial Collateral Ligament Cell Culture. The Endocrine Society 85th Annual meeting, Philadelphia, PA 2003
72. L-C. C. Yeh, R. Unda, R. Vogt, A. T. Tsin, and J. C. Lee. Insulin altered expression of the TGF- β superfamily members in human retinal epithelial cell cultures. Experimental Biology meeting, San Diego, CA 2003

73. Tsin, A.T.C., Vogt, R.R., Unda, R., and Lee, J.C. Glucose mediated regulation of bone morphogenetic protein-4 in human RPE cells. ARVO annual meeting, FL 2003

4. **Other (e.g. letters to the editor, invited lectures):**

Invited Lectures:

Have given about 60 invited lectures at national/international conferences and universities within the last 10 years.

5. **Papers Submitted/in preparation:**

Yeh, L-C. C. and Lee, J. C. *Effects of basic fibroblast growth factor (FGF) on gene expression of the rat insulin-like growth factors and their binding protein in OP-1-induced FRC cell.* **Molecular & Cellular Endocrinology.**

Yeh, L-C. C. and Lee, J. C. *Osteogenic Protein-1 stimulates PDGF mRNA expression in FRC cells.* **Endocrinology**

Unda, R., Ghaffari, S., Villazana, E., Yeh, L-C. C., Ma, J-X., Tsin, A., Lee, J.C. *Differential Characterization of ARPE 19 Cells Grown under High and Low Glucose Concentrations.* **Investigative Ophthalmology & Visual Science**

Zavala, M., Yeh, L-C. C., Lee, J.C. *Biochemical Studies on the Extracellular Ligand Binding Domain of the BMP-Type II Receptor.* **J. Biol. Chem.**

Tsai, A. D., Yeh, L-C. C., and Lee, J.C. Effects of Cartilage-derived morphogenetic proteins on gene expression of C2C12 cells

Chen, J., Tsai, A. D., Yeh, L-C. C., and Lee, J.C. Differential induction of gene expression in cultured Achille Tendon cells by Osteogenic Protein-1

B. Areas of Research Interest

Structure and function of Nucleic Acids
Regulation of eukaryotic Gene Expression
Ribosome Structure and Function
RNA-protein Interaction
Mechanism of action of osteogenic proteins

C. Current Projects:

Structure, function and dynamics of yeast ribosomes
5S ribosomal RNA-protein interaction
Structure, function and processing of yeast precursor ribosomal RNA
Molecular mechanism of action of OP-1

D. Research Support (Grants and Contracts):

Currently funded with an annual research budget of about \$300,000 US

IV. SERVICES

A. Professional Affiliations:

1) Current Professional and Scientific Organizations and Societies (*election to membership)

1966 - present	*American Chemical Society
1972 - present	*American Society of Biological Chemistry & Molecular Biology
1987 - present	American Association for the Advancement of Science
1995 - present	*American Society of Bone & Mineral Research
1996 - present	*Endocrinology Society
2001 - present	*Orthopaedic Research Society

2) Past and Current Positions and/or Offices Held in Professional Organizations: None

3) Other Professional Activities:

1988 - present	Scientific Consultant, Stryker Biotech, Hopkinton, MA
1995 - present	Reviewer of grants for North Carolina Biotechnology Research Foundation
1992	Ad hoc reviewer, Biochemistry Study Section, NIH
1976 - present	Ad hoc reviewer of grants submitted to the National Science Foundation Biochemistry Section
1975 - present	Reviewer of manuscripts submitted to the following scientific journals: Analytical Biochemistry, Biochemical Pharmacology, Biochimica et Biophysica Acta, Biochemistry, J. Molecular Biology, Nucleic Acids Research, Proc. Natl. Acad. Sci. USA, J. Agricultural & Food Chemistry, J. Bone & Mineral Research, J. Endocrinology.
2000	Grant Reviewer, Fonds zur Forderung der wissenschaftlichen Forschung, Wien, Austria
1999- 2000	Scientific Consultant, Southwest Research Institute, San Antonio, TX
1982-1986	Reviewer of Grants submitted to V.A. Central Office from Staffs of Audie Murphy Memorial V.A. Hospital at San Antonio
1980	Ad hoc reviewer of Established Investigator Awards, American Heart Association.
1976-1981,1983	Reviewer of grants submitted to American Cancer Society Institutional Grants Committee
1976	Reviewer of grants submitted to Veterans Administration Central Office from Audie Murphy Memorial Veterans Hospital
1971-1974	Reviewer of grants submitted to the University of Texas Health Science Center at San Antonio Institutional Research Grants Committee

B. Patient Service: N/A

C. Committees:

Department:

1999 - 2001	Biochemistry departmental seminar series (Coordinator)
1998	Departmental Study Group - The Graduate Curriculum (Member)
1985 - present	Departmental Tenure and promotion Committee (Member)

1995	Departmental Tenure and Promotion Committee (Chair)
1993	Ad hoc Graduate Curriculum Committee (Member)
1991 - 1992	Faculty Search Committee (Member)
1987, 1990	Promotion and Tenure Committee (Chair)
1983 - 1985	Seminar Series (Coordinator)
1978 - 1982	Committee on Graduate Studies (Member)
1979 - 1982	First Year Committee for Supervising First Year Graduate Students, (Member)
1977 - 1979	Departmental Seminar Committee (Chair)

School:

2002-present	Preclinical Promotion Committee (Member)
1996-1998	Learning Resources Planning Committee (Member)
1995-1997	Dental School Research Committee (Member)
1995	Medical School Strategic Planning subcommittee (Member)
1995	LCME subcommittee (Member)
1991-1993	Committee on Core Curriculum (Chair)
1987-1989	Committee on Committees - Dental School (Chair)
1986-1987	Committee on Committees - Medical School (Member)
1985-1987	Dental School Research Committee (Member)
1985-1987	Medical Scientist Training Program (Member)
1976-1981	Cancer Coordinating Committee - Medical School (Member)
1976-1979	Curriculum Review Committee - Medical School (Member)
1978	Subcommittee of Curriculum Review Comm. on Genetics - Medical School (Chair)
1978	Nominating Committee of Faculty Assembly - Medical School (Member)
1974-1975	Admissions Committee - Medical School (Member)
1974-1975	Nutrition Task Force - Dental School (Member)

University:

2000 – 2003	Physical Safety Committee (Member)
1988-1991	University-Industry Cooperation Research Center (Member)
1979-1981	Bio-safety Committee (Member)
1976	Research and Development Committee (Veterans Hospital) (Member)
1975-1978	Genetic Task Force (Member)
1973-1975	Pulmonary Task Force (Member)
1971-1974	Institutional Research Grants Committee (Member)